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Assessing the Impact of Body Weight on Male and Female Pubertal Development

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EPA Special Study

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Overview

- Present data from food restriction study
- Discuss results of previous studies using male and female pubertal protocols.
- Discuss examples of published data and conclusions evaluating the role of body weight and growth on pubertal events.

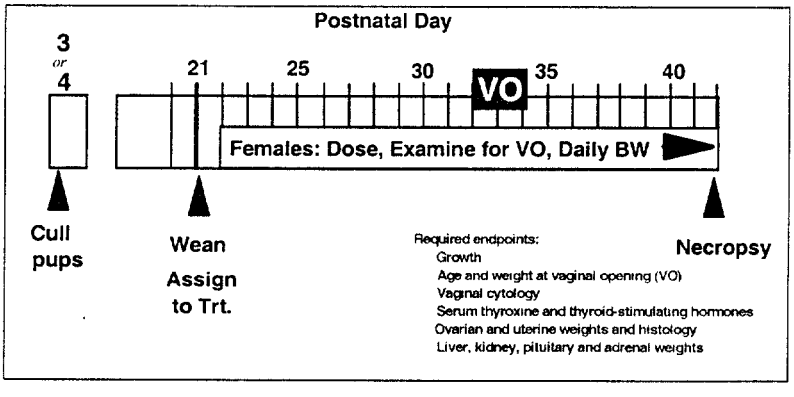
Study Objectives

- Assess the relationship between growth rate and pubertal development
- Determine whether or not reduced body weights over a range of 2 – 20% confound the endpoints in the Female and Male Pubertal Protocols

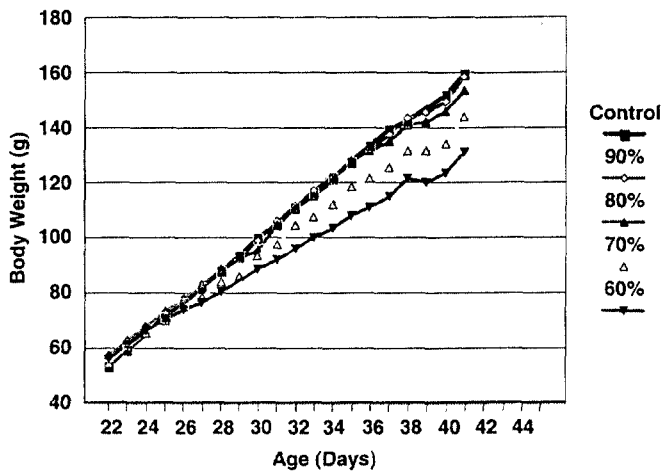
Methods

- Four groups of male and female Wistar rats (n=13) were fed 90%, 80%, 70% and 60% of *ad libitum* controls
- Pecentages were based on 24 h food intake of controls.

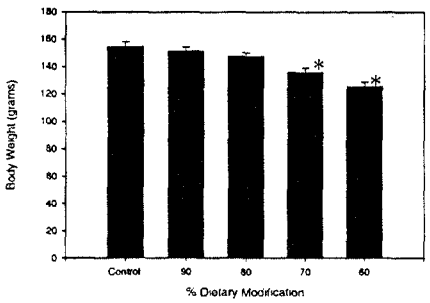
Female Pubertal Protocol



Body Weight: Female Wistar Rats



Body Weight at Necropsy Female Pubertal Study

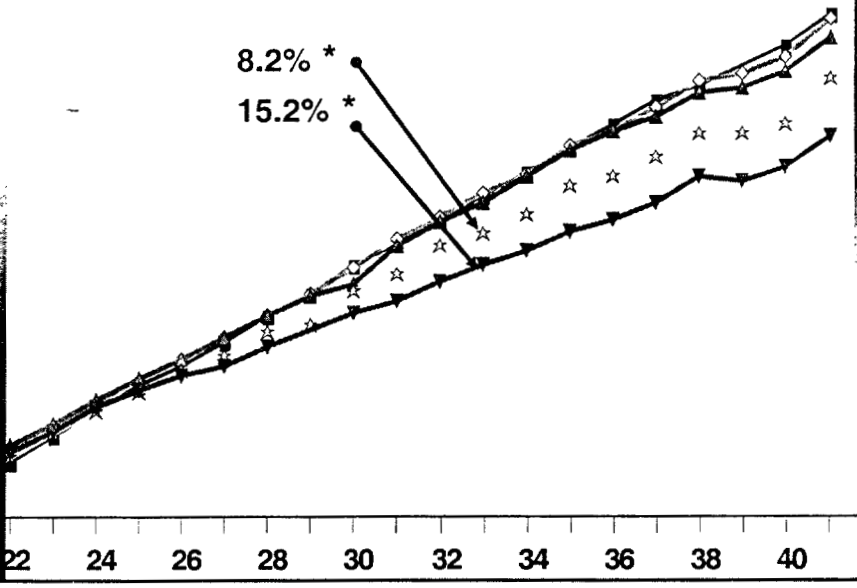


Mean +/- SEM (n=13): * P<0.05

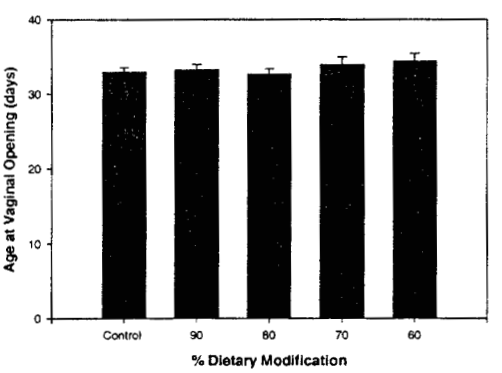
Percent reduction in BW as compared with control

- **Group 90 (2.0%)**
- **Group 80 (4.6%)**
- **Group 70 (12.1%)**
- **Group 60 (18.8%)**

Reduction in BW on PND 33

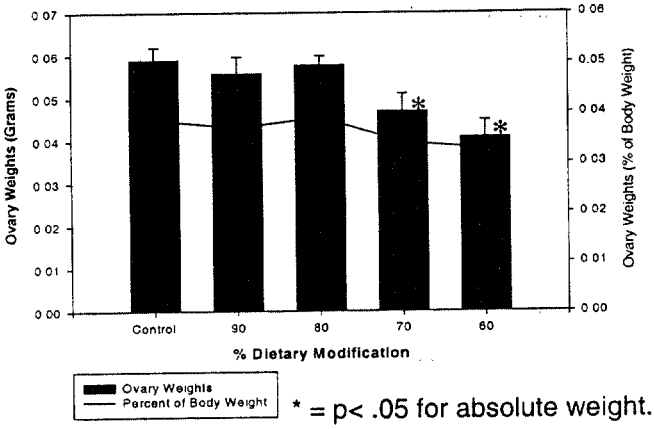


Age at VO



Group	Con	90%	80%	70%	60%
Mean	33	33.3	32.7	34.0	34.5
SEM	0.56	0.67	0.70	0.97	0.97

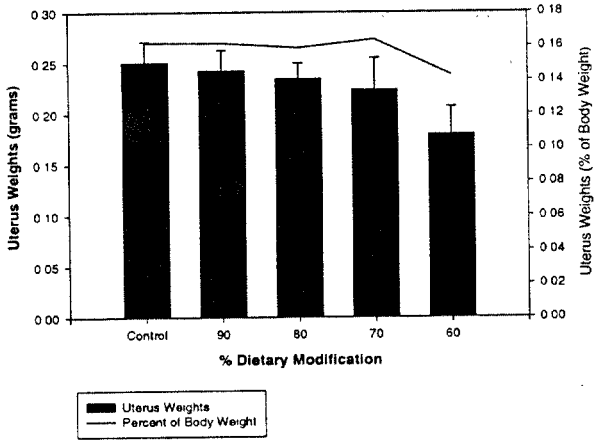
Ovary Weight



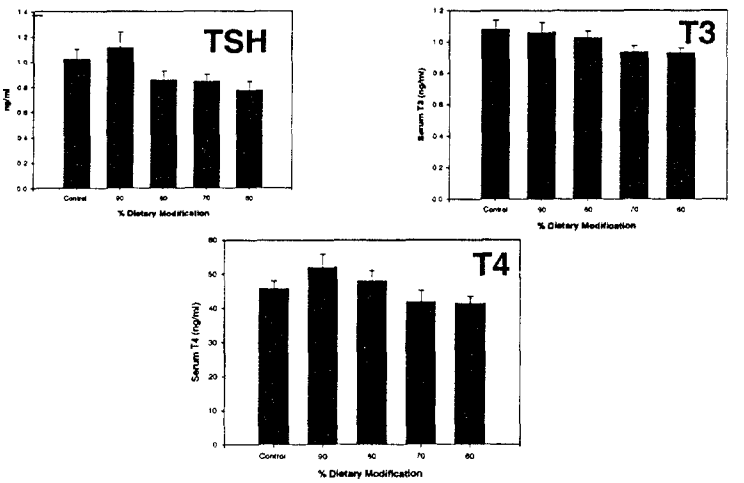
* = p< .05 for absolute weight.

r = p< .05 for relative weight.

Uterus Weight



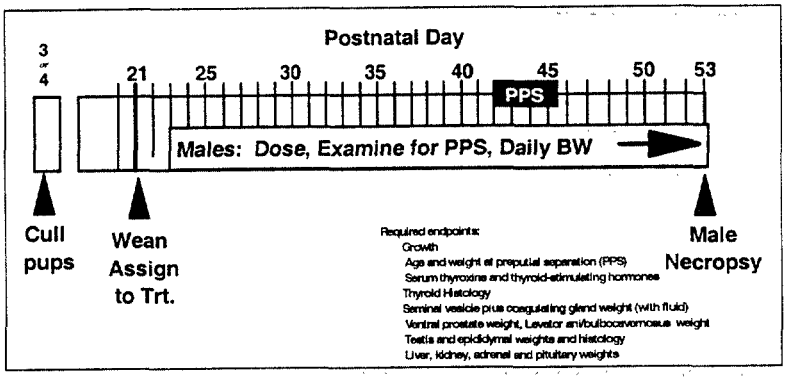
Thyroid Hormones: Female



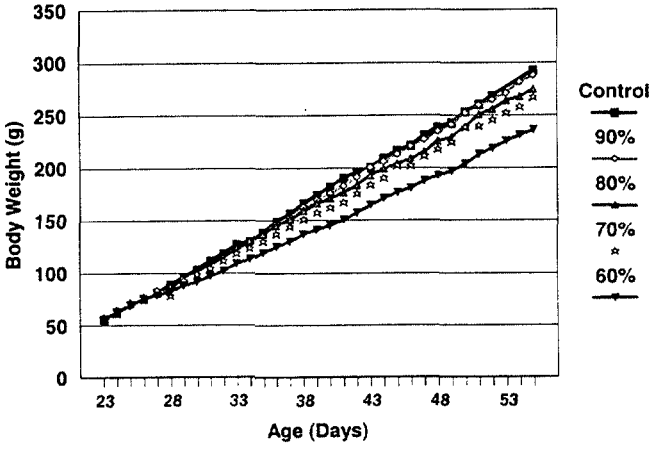
Summary of Female

- Reduced body weight gains from 2.0 to 18.8% (at necropsy)
  - no effect on VO, uterine weights or thyroid hormones
- Body weight decreases of 12.1 and 18.8%
  - decreased ovarian weight
- Importantly, there were no significant differences in any of the female reproductive endpoints at less than 12.1% decreased body weight.

Male Pubertal Protocol



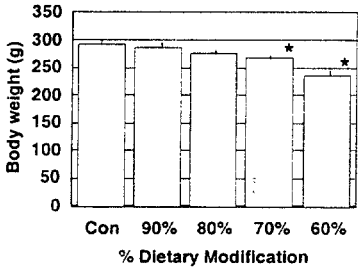
Body Weight: Male Wistar Rats



Body Weight at Necropsy: Male Wistar Rats

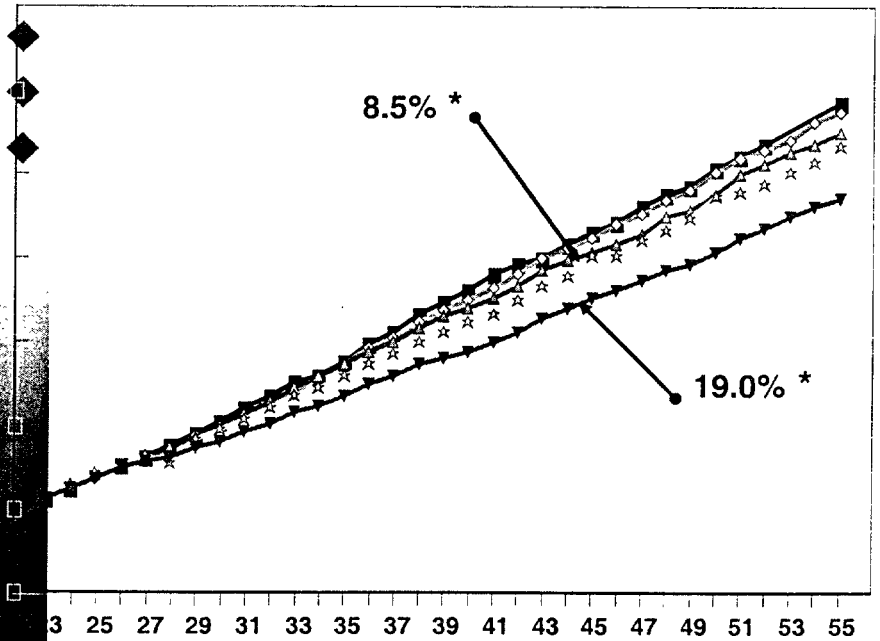
Percent reduction in BW as compared with control

- Group 90 (2.2%)
- Group 80 (4.4%)
- Group 70 (12.5%)
- Group 60 (20.7%)

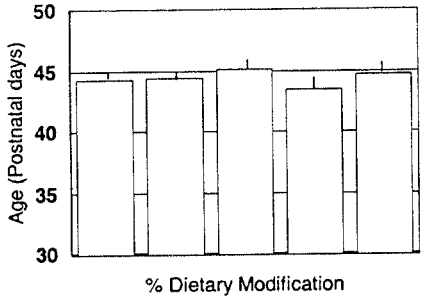


	Con	90%	80%	70%	60%
Mean	293.3	287.9	275.9	266.9	236.3
SEM	2.29	1.08	2.30	1.43	1.06

Reduction in BW on PND 44

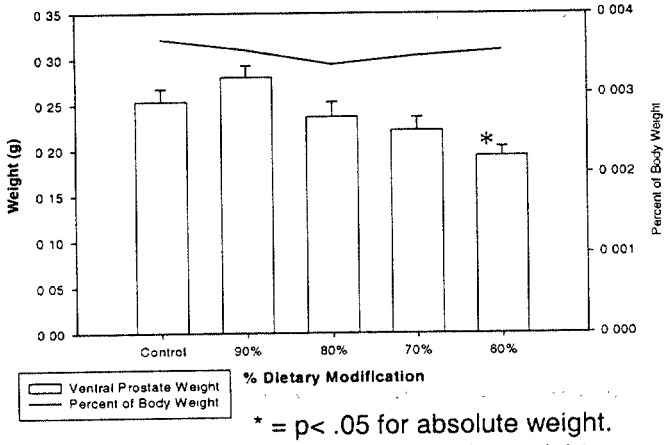


Age at Preputial Separation



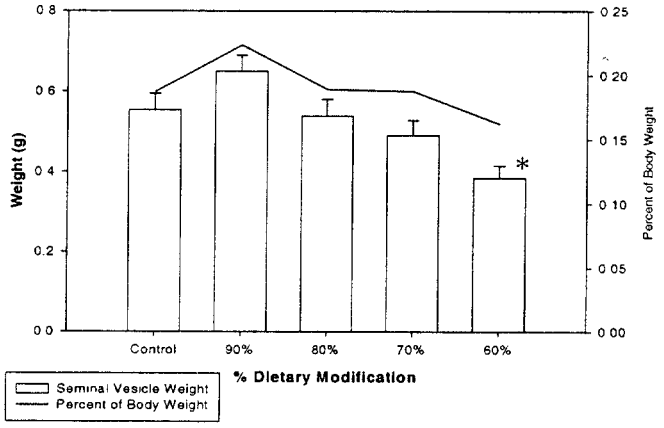
Group	Con	90%	80%	70%	60%
Mean	44.3	44.4	45.2	43.5	44.7
SEM	0.55	0.62	0.57	0.75	0.61

Ventral Prostate Weight

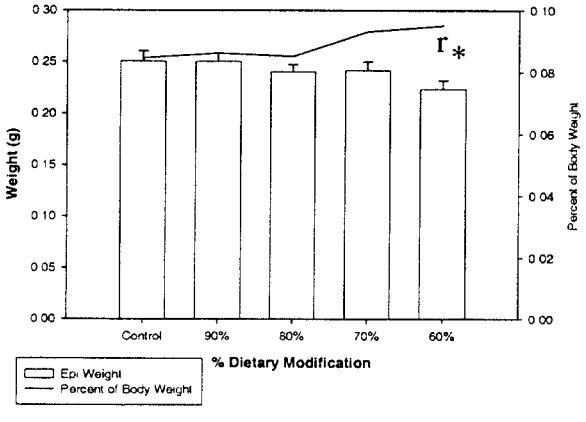


* = p< .05 for absolute weight.
r = p< .05 for relative weight.

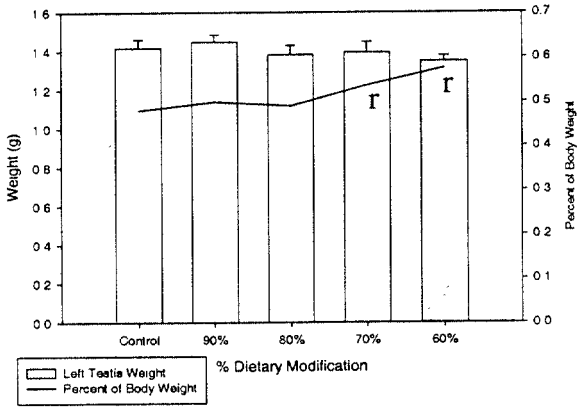
Seminal Vesicle Weight



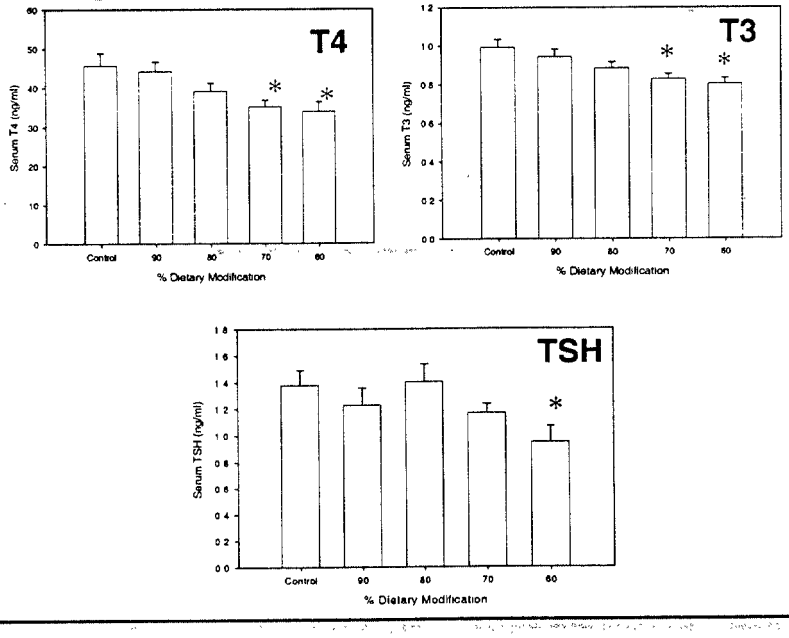
Epididymis Weight



Testes Weight



Thyroid Hormones-Male

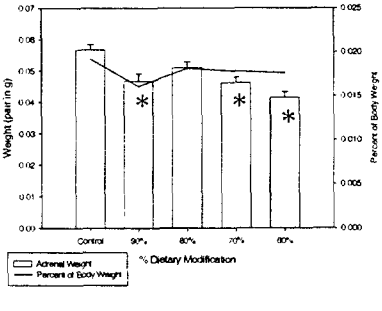


Male Summary

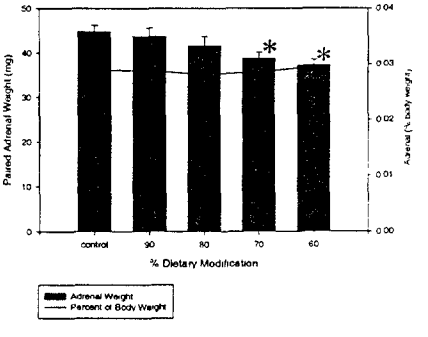
- Reductions in body weight gain from 2.2 to 20.7% had
  - no effect on PPS or testes weight
- Decreases in body weight from 12.5 to 20.7%
  - decreased T3 and T4
- Decreases in body weight of 20.7%
  - decreased ventral prostate, seminal vesicle and epididymal weights
- Importantly, there were no significant alterations of the male reproductive endpoints at decreases of less than 12.5%.

Adrenal Weights

Male



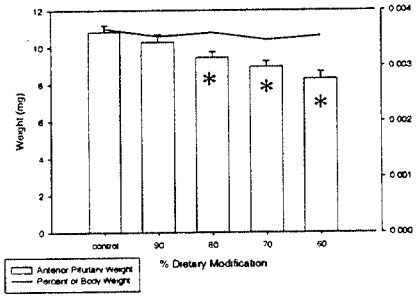
Female



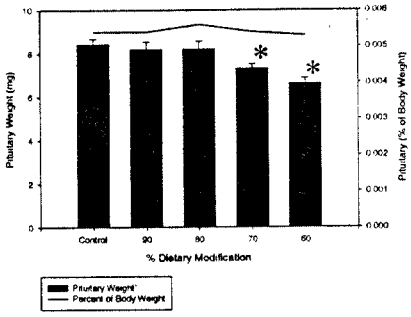
* = p< .05 for absolute weight.
r = p< .05 for relative weight.

Anterior Pituitary Weight

Male

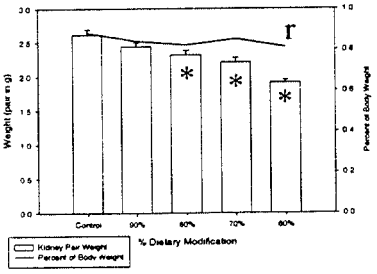


Female

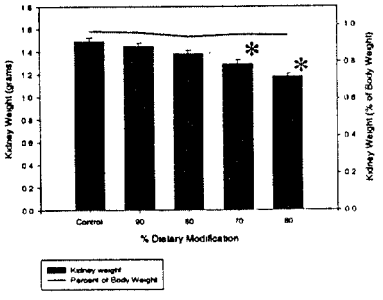


Kidney Weights

Males

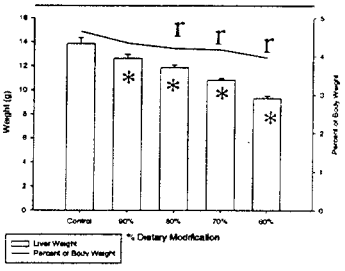


Females

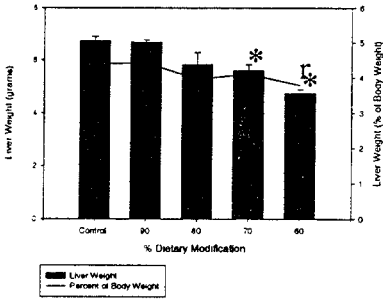


Liver Weight

Males



Females



Study Conclusions

- A 10% reduction in body weight has no effect on pubertal development
- Pubertal protocols detect a wide variety of EDCs apart from modest decreases in BW

Background Literature

- **Studies were designed to retard reproductive senescence and prolong lifespan:**
  - Litter alterations during early postnatal days resulted in 30 - 65% bw difference.
  - Other studies severely restricted food intake at weaning.
  - Indeed, these studies found that puberty was delayed.
  - The first week of life is critical for nourishment and setting of adult bw.

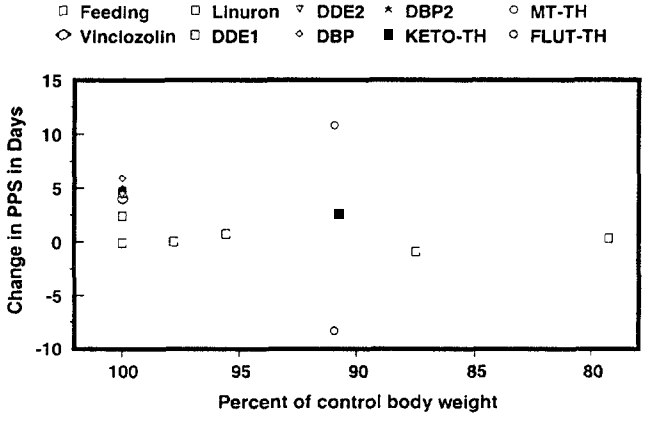
Continued:

- "attainment of critical bw" hypothesis
- "critical body fat" hypothesis
- "growth rate" hypothesis
- All have been questioned by more recent investigations which were unable to repeat earlier studies(Aguilar et al.,1984; Glass et al., 1984, Ronnekleiv, Ojeda & McCann, 1978;Bronson, 2001; Crawford and Osler, 1975).

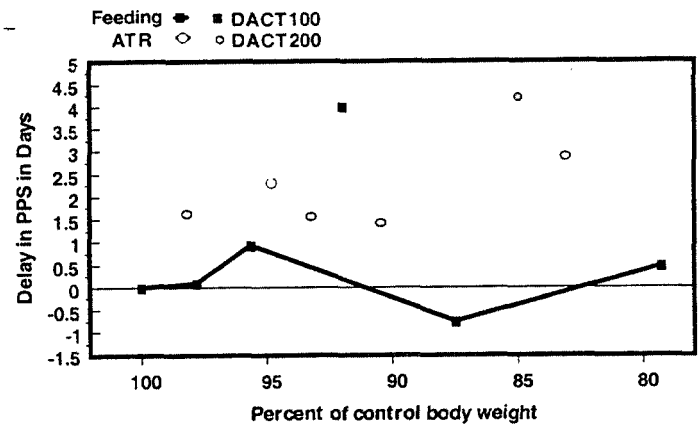
General agreement in literature

- A 10% decrease in body weight gain in the pubertal assays does not appear to confound the selected endpoints (Connor et al., 2000).
- The reproductive systems in the adult male and female rat are relatively resistant to body weight reductions down to 70% of control (Chapin et al., 1993).

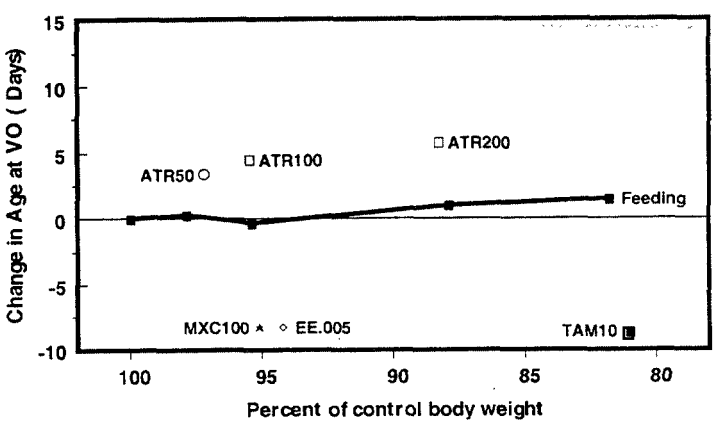
Relationship between reduction in body weight versus change in age at PPS



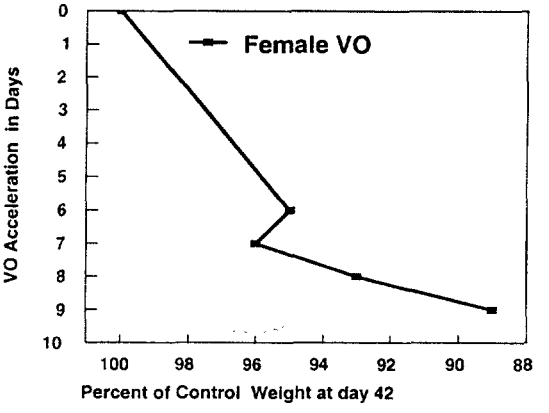
Relationship between reduction in body weight versus age at PPS



Relationship Between Body Weight and Age at Vaginal Opening



Does the estrogen mediated suppression of appetite confound the detection of VO?



Methoxychlor (0, 25, 50, 100, 200 mg/kg)

Acknowledgments

- Collaborators
  - Susan Laws, Ph.D.
  - Ralph Cooper, Ph.D.
  - Earl Gray, Ph.D.
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  - Kate Bremser
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